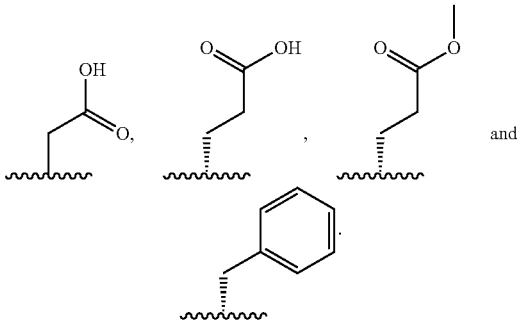
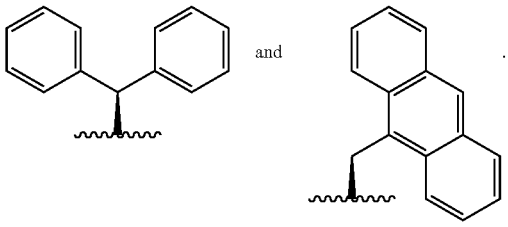
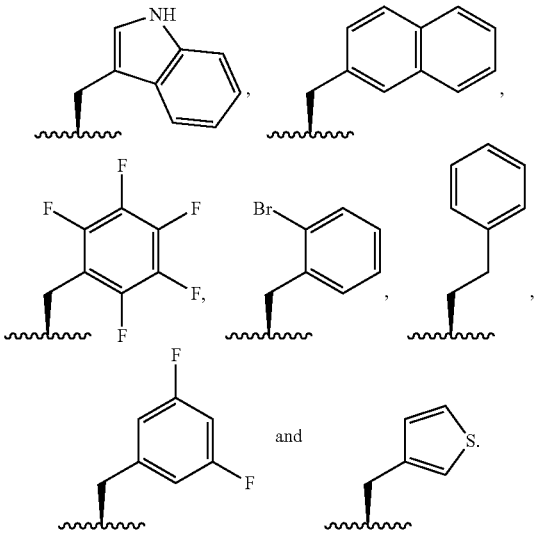


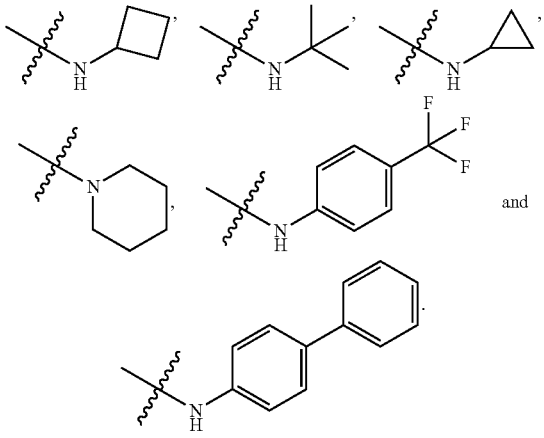
[0010] In some embodiments, R_3, is an optionally substituted aralkyl, a ketone or an optionally substituted heteroaralkyl except for



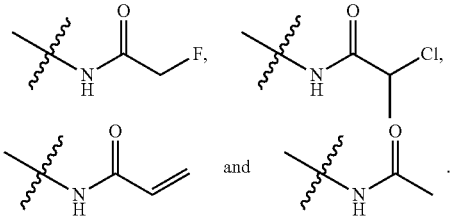
[0011] In some embodiments, R_4, is an alkyl urea, an alkyl guanidine, a hydroxyalkyl, an amide, an optionally substituted heteroaralkyl or an optionally substituted aralkyl except for



[0012] In some embodiments, R_5, is an optionally substituted N-aralkyl, an alkoxy, an optionally substituted N-methyl-aralkyl, an optionally substituted N-methyl-aryl, an optionally substituted N-aryl, an optionally substituted N-cyclyl, an optionally substituted heterocyclyl or an N-alkyl except for



[0013] In some embodiments, R_6, is a sulfonamide or an amide except for



[0014] Another aspect of the present invention is directed to a pharmaceutical composition that includes a therapeutically effective amount of a compound of the invention and a pharmaceutically acceptable carrier.

[0015] A further aspect of the present invention is directed to a method for making a compound of the invention.

[0016] Another aspect of the present invention is directed to a method of treating a disease or disorder mediated by dysregulated Pin1 activity, comprising administering a therapeutically effective amount of the compound of the invention or pharmaceutically acceptable salt or stereoisomer of to a subject in need thereof.

[0017] In some embodiments, the disease or disorder is cancer, inflammation, an autoimmune disorder or a neurodegenerative disease

[0018] In some embodiments, the autoimmune disease that is treated is lupus, asthma or arthritis.

[0019] In some embodiments, the neurodegenerative disease is Alzheimer's disease or Parkinson's disease.

[0020] Unlike many previously identified Pin1 inhibitors, many of the Pin1 inhibitors disclosed herein are cell permeable. The present invention provides peptidomimetic inhibitors, many of which irreversibly bind to Pint's cysteine 113, located in the PPIase active site. Thus, the compounds disclosed herein are selective, potent and cell permeable irreversible Pin1 inhibitors.

[0021] Without intending to be bound by any particular theory of operation, it is believed that compounds of the present invention exhibit their inhibitory activity by binding to at least one amino residue, e.g. cysteine 113, located in the active site of Pin1. Without intending to be bound by any theory of operation, Applicant believes that the compounds